

### **Section III (Remarks)**

#### **A. Summary of Amendment to the Claims**

By the present Amendment, claims 1-45 have been cancelled; and new claims 46-56 have been added.

The amendments made herein are fully consistent with and supported by the originally-filed disclosure of this application. Specifically, new claim 46 is supported by original claim 12, new claim 47 is supported by original claim 2, new claim 48 is supported by original claim 13, new claim 49 is supported by original claim 4, new claim 50 is supported by original claim 14, new claim 51 is supported by original claim 15, new claim 52 is supported by original claim 16, new claim 53 is supported by original claim 17, new claim 54 is supported by original claim 18, and new claim 55 is supported by original claim 45.

No new matter within the meaning of 35 U.S.C. §132(a) has been introduced by the foregoing amendments.

#### **B. Rejection of Claims Under 35 U.S.C. §103(a)**

In the May 20, 2008 Office Action, the examiner rejected claims 2, 4, 12-18 and 45 under 35 U.S.C. §103(a) as being unpatentable over the combination of U.S. Patent No. 5,922,183 (hereinafter “Rauh”) in view of Bu et al., *Anal. Chem.*, 1995, 58, vol. 22, 3951-3957 (hereinafter “Bu”). All such rejected claims have been cancelled herein.

Such rejection is traversed in application to claims 46-56 newly added herein.

It is elemental law that in order for an invention to be obvious, the difference between the subject matter of the application and the prior art must be such that the subject matter as a whole would have been obvious at the time the invention was made to a person of ordinary skill in the art. In order to meet this standard for a proper §103 rejection, all claim limitations must be disclosed or derivable from the cited combination of references, there must be a logical reason to combine the cited references to produce an operable combination and there must be a reasonable expectation of success. (MPEP §2143)

The examiner's attention is respectfully drawn to newly added independent claim 46 above, which recites:

46. An electrically non-conductive, nanoparticulate membrane comprising nanoparticles of at least one inorganic oxide of an element selected from Group IA, IIA, IIIA, IVA, IB, IIB, IIIB, IVAB, VB, VIB, VIIB or VIIIB of the Periodic Table, and wherein an oxidoreductase enzyme and a polymeric redox mediator capable of transferring electrons are diffusibly dispersed in said nanoparticulate membrane.

Particularly the examiner's attention is respectfully drawn to the recited elements of the nanoparticulate membrane and the characteristic of "diffusibly dispersed" of claim 46. All remaining pending claims depend directly or indirectly from claim 46. Accordingly, all of claims 47-56 also contain the elements of a "nanoparticulate membrane" and "diffusibly dispersed." These elements have no derivative basis in the cited combination of Rauh in view of Bu et al. and therefore the combination of references does not render the claimed invention obvious.

The nanoparticulate membrane of applicants' invention is described throughout the application. It is prepared from a nanocompatible slurry ink that is deposited onto a substrate (para. [0015], [0063], [0066], [0067], and [0068]). As claimed, the nanoparticulate membrane comprises nanoparticles of at least one inorganic oxide of an element selected from Group IA, IIA, IIIA, IVA, IB, IIB, IIIB, IVB, VB, VIB, VIIB, VIIIB and where an oxidoreductase enzyme and a polymeric redox mediator are diffusibly dispersed in the membrane.

Rauh discloses a thin film matrix for biomolecules comprising an oxidoreductase that may also comprise an additional electron transfer relay, which may be incorporated by polymerization (col. 5, ll. 30-33). The matrix disclosed in Rauh consists of hydrous metal oxide (see Fig. 1 and Example 1 of Rauh). The matrix of Rauh is generated from "composite layers of conducting/semiconducting hydrous metal oxides and biomolecules..." or by electrodeposit (col. 4, ll. 41-44; 62-65). The matrix is impregnated with glucose oxidase, by a process during which the enzyme is stated to become trapped in the oxide matrix (see Example 1, and in particular column 12, line 35 of Rauh). Also, as the examiner has pointed out, Rauh state that "...[a]dditional electron transfer mediators can be co-immobilized into the oxide matrix..." (col. 8, ll. 66-67; emphasis added). Glucose oxidase is therefore not diffusibly dispersed in the Rauh matrix and Rauh therefore does not disclose a nanoparticulate membrane as claimed by

applicant. Rauh fails to disclose a respective diffusible dispersion as required by applicants' claims.

Further, Rauh teaches that the thin film matrix described therein possesses a number of advantages, including being inherently stable under physiological conditions (col. 3, l. 43 et seq. and col. 4, l. 14 et seq.) and protecting an enzyme from deactivation over extended storage (col. 3, l. 65 et seq. and col. 4, l. 14 et seq.). Therefore one of ordinary skill in the art is led to conclude that Rauh successfully achieves prolonged periods of storage of the disclosed thin film matrix and one of ordinary skill in the art therefore would not be motivated to alter the characteristics of the matrix, when a successful product has already been achieved.

The Rauh reference thus fails to disclose a nanoparticulate membrane and furthermore does not disclose that glucose oxidase or any other polymeric redox mediator capable of transferring electrons is diffusibly dispersed in the matrix. Furthermore, the membrane as claimed is stable even under prolonged periods of storage. The provisions of the Bu et al. reference fail to remedy the deficiencies of the Rauh reference.

Rauh viewed in light of Bu et al. also does not provide a diffusibly dispersed oxidoreductase enzyme and polymeric redox mediator capable of transferring electrons in a nanoparticulate membrane, as recited in the claims of the present invention.

Bu et al. also does not describe a nanoparticulate membrane as claimed. At page 3952 left col., 2<sup>nd</sup> paragraph, lines 12 to 14; right col., 2<sup>nd</sup> paragraph, lines 8 to 12 and in particular page 3953, left. col., "Results and Discussion" lines 6 to 13, describe that VF (a copolymerization of N-isopropylacrylamide with vinylferrocene (p.3952, left. col., lines 4-5)) copolymerizes with AA and BIS in aqueous solution. However, such co-polymerization means that the redox-polymer referred to in the Bu et al. reference is immobilized and is not diffusibly dispersed, as recited in the claims of applicants' invention.

Additionally, see Bu et al. at page 3953 (right col., "Characterization of Charge Transfer") where "*electron hopping*" via "*fixed redox-active VF residues*" is described. Thus, the redox polymer discussed in the Bu et al. reference is present in a fixed position and is not diffusibly dispersed as required by applicants' claim 46, and claims dependent therefrom.

Therefore, a combination of the disclosures of Rauh and Bu et al. cannot yield applicants' claimed invention, since the combination of references does not provide all elements of the claimed invention. For such reasons, new claims 46-56 are patentably differentiated over the combination of Rauh and Bu et al.

**C. Rejection of Claims Under 35 U.S.C. §112, First and Second Paragraph**

Claims 2, 4, 12-18 and 45 were rejected by the examiner under 35 U.S.C. §112, first paragraph for the stated reason that the specification, while being enabling for specific electron mediators, does not reasonably provide enablement for "an electrochemical activator." See page 4 of the Office Action.

While claims 2, 4, 12-18 and 45 have been cancelled by the present Response, the rejections will be discussed below as applicable to the presently pending claims.

In paragraph 2 at page 2 of the May 20, 2008 Office Action, the examiner stated that novelty of applicants' disclosed invention "may" reside in making vinylferrocene acrylamide copolymers for glucose sensors where the ferrocene does not interfere with the polymerization while in sufficiently high concentration.

On page 4 of the Office Action mailed May 20, 2008, the examiner has rejected the claims alleging that the specification does not contain enablement for the phrase "an electrochemical activator." New claims 46-56 do not contain such recitation, but instead recite "a polymeric redox mediator capable of transferring electrons" consistent with the language of previously pending claim 13. New claim 48 recites "a vinylferrocene-based polymeric redox mediator capable of transferring electrons," consistent with the disclosure at page 9, paragraph [0042] of the specification.

New claim 56 recites specific polymeric redox mediators, consistent with the disclosure of paragraph [0044], at page 10 of the specification.

The term "polymeric redox mediator capable of transferring electrons" is clear and definite and fully enabled. The specification of the present application provides sufficient information for one of skill in the art to know and utilize such redox mediator molecules. For example in

paragraph [0002] it is said that conduction polymers and charge transfer polymers are already known in the art to be suitable as electron transfer molecules. Such polymeric redox mediators capable of transferring electrons are therefore readily identifiable within the skill of the art, without undue experimentation.

Additionally, claims 2, 4, 12-18 and 45 were rejected under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

No presently pending claims contain the phrase “electrochemical activator.” This rejection is therefore moot.

New claim 46 contains the language “...at least one inorganic oxide of an element selected from Group IA, IIA, IIIA, IVA, IB, IIB, IIIB, IVAB, VB, VIB, VIIB or VIIIB of the Periodic Table...” The examiner has alleged that this language is “improper Markush terminology. Applicants respectfully disagree. The examiner’s attention is respectfully drawn to MPEP 2173.05(h), a section titled “Alternative Limitations.” Under “II. ‘OR’ TERMINOLOGY” it is stated that “[a]lternative expressions using ‘or’ are acceptable, such as ‘wherein R is A, B, C, or D.’” The above language properly includes such “or” terminology and is submitted as in compliance with the requirements of 35 U.S.C. §112, second paragraph.

The examiner also rejects claim 13 as containing the phrase “capable of.” The phrase “capable of,” now present in claim 46, is a fully proper term in referring to electron transfer molecules. A search made on November 19, 2008 of issued U.S. patents whose claims contain the phrase “capable of” (at the search site <http://patft.uspto.gov/netahtml/PTO/search-adv.htm>) gave the following result:

**“Results of Search in US Patent Collection db for:**

**ACLM/“capable of”:** 245405 patents.

*Hits 1 through 50 out of 245405”*

Since there are currently approximately 7.45 million U.S. patents issued, the percentage of U.S. patents whose claims contain this phrase is ~3.3% of all U.S. patents. Further, 277 patents containing such claim language issued on November 18, 2008, as determined from these search

results, thereby evidencing that such language is routinely accepted and allowable in U.S. patent claims.

Additionally the examiner rejects claim 15, stating that “the units are not understood.” Clarification of this rejection is respectfully requested. In previously pending claim 15 and presently pending claim 51 recite a membrane of thickness “250 to 500  $\mu\text{m}$ .” It is submitted that “ $\mu\text{m}$ ,” as an abbreviation for “micrometers” and defined as  $1/10^6$  meters is well known in science and, as used in the claims is definite under the requirements of 35 U.S.C. §112.

It therefore is requested that the rejections under 35 U.S.C. §112, second paragraph be withdrawn.

#### **D. Objection to Title of the Invention and Abstract of Disclosure**

In the May 20, 2008 Office Action, the examiner objected to the title of the application. The title has been responsively amended.

In response to the objection to the abstract of the disclosure, applicant has amended the abstract of the disclosure in Appendix A hereof.

#### **C. Fee Payable for Three Months Extension of Time**

As previously indicated, the time for responding to the May 20, 2008 Office Action without extension was set at three months, or August 20, 2008. Applicants hereby request a three month extension of time under 37 CFR § 1.136 to extend the deadline for response to November 20, 2008. Payment of the \$1,110.00 large entity fee specified in 37 CFR § 1.17(a) is hereby made by online credit card authorization.

### **CONCLUSION**

Based on the foregoing, all of Applicants’ pending claims 46-56 are patentably distinguished over the art, and in form and condition for allowance. The examiner is requested to favorably consider the foregoing, and to responsively issue a Notice of Allowance. If any issues require

further resolution, the examiner is requested to contact the undersigned attorney at (919) 419-9350 to discuss same.

Respectfully submitted,

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Enclosures:  
Appendix A [2 pgs.]

<p>The USPTO is hereby authorized to charge any deficiency or credit any overpayment of fees properly payable for this document to Deposit Account No. 08-3284</p>
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# APPENDIX A